

REMARKS

Prior to this amendment, claims 1-14 were pending, claims 11-12 canceled, and claims 13-14 withdrawn. Claims 1 and 4 have been amended. No new matter is added. Claim 3 is canceled. Applicants respectfully request reconsideration of the rejections and allowance of claims 1-2 and 4-10, the presently pending claims.

Claims 1-10 and 13 have been rejected under 35 U.S.C. 112, first paragraph. The Office Action states that the specification does not enable a person skilled in the art to practice the invention commensurate in scope with the claims. Applicants respectfully submit that the presently claimed invention meets the requirements of 35 U.S.C. 112. The present claims are drawn to a method of treating cutaneous inflammation in a subject using an small molecule inhibitor of integrin linked kinase (ILK).

The rejection is based on a consideration of the factors raised by *In re Wands*, which Applicants will address herein. The Office Action asserts that the "nature of the invention is extremely complex in that it encompasses the actual determination of what is a small organic molecule". Applicant submits that the invention is not excessively complex, with the following explanation.

The instant specification teaches the identification of integrin-linked kinase, specific compounds that inhibit the kinase, methods of screening for inhibitory agents, and methods of administration.

Applicants respectfully submit that the specification and the amended claims, coupled with the information known in the art, would enable one of skill in the art to use the invention without undue experimentation. Relevant enablement factors are discussed in detail below.

The courts have clearly taught that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. For example, see MPEP §2164.01.¹

As the court explained²:

"[A] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed."

Practitioners in the chemical and molecular biology arts frequently engage in extensive modification of reaction conditions and complex and lengthy experimentation where many factors must be varied to succeed in performing an experiment or in producing a desired result. The Federal Circuit has found that such extensive experimentation is not undue in the molecular biology arts. For example, the court concluded that extensive screening experiments, while being voluminous, were not undue in view of the art, which routinely performs such long experiments.³

With respect to the breadth of the claims, the breadth is commensurate with the scope of the invention in light of what was previously known. It is believed that the applicant is entitled to this scope for this reason.

With respect to guidance of the specification, applicant respectfully disagrees that there was inadequate guidance in the specification in light of the state of the art. With respect to the state of the art at the time of filing, there were two patent applications issued in the US on small molecular ILK inhibitors, US Patent No. 6,214,813 issued April 10, 2001, and US Patent No. 6,291,447 issued September 18, 2001. There was also a patent issued on antisense constructs, namely US 6,177,273. In addition, high throughput screening techniques were well known at the time of filing, and high throughput screening for inhibitors of ILK have been described (See US Patent No. 6,214,813 columns 15-18). In addition, small molecule libraries were available for purchase from companies such as Talon Cheminformatics (Acton, Ontario) and Asinex (Moscow, Russia), providing a source of small molecules for screening.

Screening programs have been shown to result in the identification of a number of inhibitors of ILK, for example those molecules described by U.S. 6,214,813 and U.S. 6,291,447. One skilled

1 See also *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985).

2 *In re Wands* 8 USPQ 2d at 1404

in the art could identify ILK inhibiting small molecules by running library compounds through an *in vitro* assay and calculating the IC₅₀ using the methods provided in US Patent No. 6,214,813.

Compliance with the enablement requirement under Section 35 U.S.C. §112, first paragraph does not require or mandate that a specific example be disclosed. The specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art would be able to practice the invention without undue experimentation.⁴ Furthermore, "Nothing more than objective enablement is required, and therefore it is irrelevant whether [a] teaching is provided through broad terminology or illustrative examples."⁵ As discussed above, several specific examples of inhibitors were available to the public.

Administration instructions are found in paragraphs 52 and 56 – 69 of the present application. Experimental models for inflammation are found at Examples 3 and 4, and for psoriasis in particular at Examples 1 and 2. The instant specification teaches the identification of integrin-linked kinase, specific compounds that inhibit the enzyme, and methods of screening for inhibitory agents, and methods of administration on pages 4-14.

In the present application, data are presented that demonstrate an oral formulation was effective to reduce symptoms of inflammatory disease in animal models. In view of this evidence, and of the level of skill in the art regarding inhibition of integrin linked kinase, one of skill in the art could readily practice the claimed invention, with no more than routine formulation skill or experimentation. A person skilled in the art would be able to take the compounds disclosed in previously discussed US Patent No. 6,214,813 (pyrazoles) and 6,291,447 (granulatimides), as well as US Patent No. 6,001,622 (wortmannin) and apply them to the claimed method, using the information supplied in those patents and in the present application on pages 6-15 and 16-17. In addition, pages 4-6 give a more general description of agents qualifying as ILK modulating agents for use in the methods of the invention.

One need only optimize dose and formulation for practice of the invention. As such, the only experimentation that may be required is to perform experiments to determine the appropriate dose of a certain activity. Since such experiments are empirical in nature, no undue experimentation is

³ *Hybritech v. Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986)

⁴ *In re Borkowski*, 164 USPQ at 645.

⁵ *In re Robins* 166 USPQ 552 at 555 (CCPA 1970).

required.

The relevant ordinarily skilled artisan is generally a skilled laboratory technician with the equivalent of a doctoral degree in molecular biology techniques. Furthermore, such technicians are required to keep abreast of the latest technology through continuing education and reading of scientific journal articles. As such, the skill level of those developing and using methods for manipulating performing cell-based assays is high.

In sum, the amount of experimentation required to inhibit or prevent inflammation using compounds that specifically inhibit integrin-linked kinase, as identified by Applicants, would not be undue because a) examples of inhibitors are provided, b) guidance is given on how to screen for additional inhibitors, and c) one of skill in the art would be able to perform the experiments as a matter of routine to determine the optimal dosage.

With respect to the working examples, the identity of MC-5 is 4-[(4-fluoro-3-trifluoromethylphenyl)hydrazone]-4H-pyrazole-3,5-diamine, a pyrazole compound. US Patent No. 6,214,813, referenced on lines 14-15 of page 5 of the present application, offers compounds with similar utility. The compounds provided in the present example were meant to illustrate the invention, but not to limit it.

The Examiner's request that the applicant review his patent portfolio to avoid double patenting has been noted. Co-pending U.S. patent application serial number 09/840,704 is directed to similar subject matter, however the current claims have been amended to limit the invention to cutaneous inflammation.

Applicants respectfully submit that the specification provides sufficient enablement to allow one of ordinary skill in the art to practice the claimed invention without undue experimentation. In view of the above amendments and remarks, withdrawal of the rejection is requested.

CONCLUSION

Applicants submit that all of the claims are now in condition for allowance, which action is requested. If the Examiner finds that a Telephone Conference would expedite the prosecution of this application, she is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any other fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No.

50-0815, order number KINE-001CIP5.

Respectfully submitted,

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